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Case Report

A case of diffuse large B-cell lymphoma clinically and pathologically confused with breast cancer

A case of lymphoma that is confused with breast cancer

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Abstract
Primary breast lymphoma is defined as only the presence of disease in the breast without in any other region of the body. Diffuse large B cell lymphoma (DLBCL) is most common among lymphoma types and accounts for approximately 50% of cases. We presented a case that was evaluated as breast cancer after initial pathological reports but diagnosed with DLBCL in further examinations. A 56-year-old woman with breast and axillary mass complaint who was initially evaluated as breast carcinoma and started treatment accordingly was presented. Due to clinical and pathological suspicion, biopsies repeated. The performed tru-cut breast biopsies were found to be compatible with DLBCL. In cases where adequate immunohistochemical examinations cannot be performed or there are conflicting data in the pathology reports, it is very important for the differential diagnosis to be evaluated together with the clinic and in case of doubt, biopsy repeats and pathology samples are re-examined in advanced centers.

Keywords
Breast Cancer, Lymphoma, Repeated Biopsies

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Introduction

Lymphoma in the breast develops as primary or secondary. Primary breast lymphoma is defined as only the presence of disease in the breast without any other region of the body [1]. Metastatic breast lymphoma is two-three times more common than primary breast lymphoma, but response to treatment is better. Diffuse large B-cell lymphoma (DLBCL) is the most common among lymphoma types and accounts for approximately 50% of cases. There are also cases reported as follicular lymphoma, mucosa- associated lymphoid tissue (MALT) lymphoma and Burkitt's lymphoma [1-2]. In this study, we present a case that was evaluated as breast cancer after initial pathological reports in tru-cut biopsy samples taken from masses in the breast and armpit and was diagnosed with DLBCL in further examinations. We present this case with the aim of emphasizing the importance of clinical approach and pathological examinations in the differential diagnosis.

Case Report

A 56-year-old female patient was admitted to the outer center due to swelling in the right breast and armpit that she noticed in the last 1-2 months. Breast ultrasonography performed at this center showed a mass lesion of 88x54 mm that extends from the upper outer quadrant of the right breast to the axillary tail, and the right breast upper outer quadrant tru-cut biopsy is 'malignant tumoral formation and it is recommended to be evaluated in an advanced center where immunohistochemical examination can be performed for definitive diagnosis and typing'. As a result of this pathology, the patient applied to the oncology department of our hospital. There was a mass extending from the upper outer quadrant of the right breast to the axilla in physical examination of the patient. The boundary separation between the axilla and breast tissue of the mass could not be made clear, and it was about 10-12 cm in size. No additional features or additional lymphadenomegaly were detected in other system examinations. She had a chronic history of hepatitis B and hypertension and was treated with entecavir and amlodipine.

In the breast magnetic resonance imaging (MRI), a mass lesion of 130x68 mm, which indicates the extension from the right breast tail to the axilla, and a mass lesion of 50x39 mm on the upper outer quadrant of the right breast in the anterior part of this, as well as several metastatic lymph nodes with thick cortex, the largest of which was 42x27 mm, were detected in the right axillary area. Positron emission tomography (PET) imaging showed a mass lesion with increased fluorodeoxyglucose (FDG) involvement of 112x54 mm (suvmax: 31.9) indicating extending to the nipple in the right axillary region and lymph nodes with a large size of 22x10 mm in the right axillary area and slightly increased FDG involvement in the large lymph node (suvmax:3.3). With these evaluations, the outer central pathology blocks were re-examined in our hospital and a second tru-cut biopsy was performed from the breast and axial region. ER (-), PR (-), CERBB2 (-), CK7 (-), CD56 (-), CD10 (-), TTF (-), P40 (-) chromogranin (-), synaptophysin (-), Ki-67 %80 (+) were detected in the examination of external central pathology blocks. The pathology report stated that 'the tumor consists of atypical epithelial cell plates with large hyperchromatic nucleus, high mitosis and apoptosis, and carcinoma infiltration primarily brings to mind low differential/high grade invasive ductal carcinoma'. With these findings, neoadjuvant chemotherapy cyclophosphamide + doxorubicin treatment was started and the second biopsy result was planned to be followed up in our hospital.

The pathology report of the repeated breast tru-cut biopsy shows tissues of the lymph node, larger size lymphocytes forming nodular structures separated from the environment by a sharp boundary, and small-sized lymphocytes surrounding them are monitored. When the case was evaluated together with immunohistochemical studies, it was thought that the samples may primarily belong to the lymph node of intramammarian reactive properties due to the fact that the nodular structures are separated from the environment by the sharp boundary and contain histiocytes. Immunohistochemical examination of CD19 and CD20 follicular structures: (+), CD45 (LCA): (+) , CD79a (+) , pax5 follicular structures: (+) , c-myc 10-15% (+) ki67 1-2 % (+). Reactive lymphoid tissue fragments containing lymphocytes and histiocytes were observed in the tru-cut biopsy of the axillary region. Cytokeratin was negative and CD3, CD20 and Ki 67 were focal (+) in the immunohistochemical examination. After these pathology reports, a re-biopsy decision was taken by discussing the pathology caused by the continued suspicion of lymphoma in the case. During this time, chemotherapy continued.

Multiple tru-cut biopsies from the right axillary region were repeated. As a result of the pathology, pan-keratin and CD45 were (+), some of the lymphocytes were (+) for CD19 and in the pathological interpretation, tissues belonging to lymph nodes with hyalinized parenchyma were seen in the sections, it was reported that small scattered lymphocytes and histiocytes are present in this parenchyma. Accordingly, although lymphoma cannot be excluded and the diagnosis of carcinoma could not be confirmed. With the final pathology report, it was planned to send all existing pathology blocks of the case to an advanced center and examine them. Meanwhile, 4 cycles of cyclophosphamide+doxorubicin chemotherapy were completed and the control breast MRI showed regression of the mass

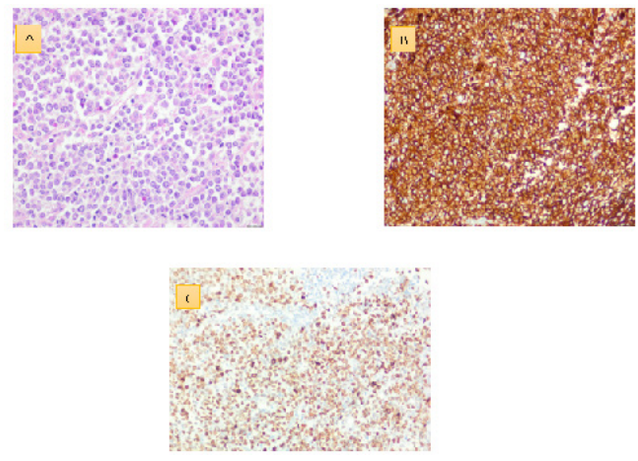

Figure 1. (A) Atypical lymphoid cells with a large nucleus, scant cytoplasm. Mitotic figures are commonly seen (H&E X400). (B) Tumour cells are diffusely positive for CD20 (x200). (C) KI 67 proliferation index reaches 95%.

lesion in the breast to 35x19 mm and axillary LAP to 13x8 mm. Advanced center pathology reports were concluded while the treatment of the case continued with weekly paclitaxel. In the pathological examinations from the advanced center, breast tru-cut biopsies performed at our center and in the hospital before the patient contacted us were found to be compatible with diffuse large B cell lymphoma (Figure 1A). CD20 and Pax5 (+) were in these reports (Figure 1B); MUM 1 and ALK(-), c-myc 25-40% nuclear staining, ki67 was 95% in the first biopsy sample (Figure 1C) and 70-80% in the next one. Axillary tru-cut biopsies taken in our hospital were reported as lymphoid infiltration in reactive and collagen fibrotic tissue. After these reports, the case was considered diffuse large B cell lymphoma and was referred to the hematology clinic. Control PET imaging showed an increased FDG overall with dimensions of 44x20 mm in the right axillaries area (suvmax 5.4) of the malignant mass lesion, according to the previous examination, regression in size and metabolic activity was observed, as well as regression in size and metabolic activity in lymph nodes with slightly increased FDG involvement (suvmax 2.4), which was approximately 12x7 mm in the right axilla. Lymph nodes with increased FDG involvement in the left hilar region (suvmax 8.2) were reported as new findings, and the treatment of R-CHOP (rituximab-cyclophosphamide, doxorubicin, vinchristine and prednisone) was planned by hematology.

Discussion

As a result of clinical and pathological evaluations of the patient's complaint of a mass in the breast and axilla, it was diagnosed as lymphoma (DLBCL), not breast carcinoma. DLBCL is the most common subtype of metastatic breast lymphoma, which is more common than primary lymphoma of the breast [1-2]. Diffuse large B-cell lymphoma accounts for approximately 30-40% of all non-Hodgkin's lymphomas in western countries. Since this group of tumors includes heterogeneous clinical, morphological, immunological and cytogenetic features, these tumors show a very variable clinical course and significant biological heterogeneity [3]. DLBCL usually expresses CD45 and pan-B (CD19, CD20, CD79a) markers. CD20 is a highly specific marker for the B cell line. However, although rare, CD20(+) peripheral T-cell lymphoma cases have been reported. In the case we have presented, in some of the biopsies repeated in our hospital and in the pathological examination performed in an advanced center, the neoplastic cells stained with CD20, CD79a, CD19 and Pax5 and diffusely positive staining and for breast origin, keratin 19, GATA-3 and ER, PR with cerbb2 and e-cadherin negative staining were found. Ki-67 is a protein and its high expression is a proliferation marker detected in the G1, G2, S and M phases of the cell cycle. In many studies, regardless of clinical variables, a high Ki-67 index (≥60-80%) in DLBCL indicates decreased total survival [4]. In our case, the Ki-67 index was reported as 80% in the examination of the first biopsy in our hospital, and 1-2% and focal (+) in two repeated biopsy examinations in our hospital. In two separate biopsy samples re-examined in the advanced center, ki-67 was detected at 95% and 80%.

Primary lymphomas of the breast are extremely rare tumors with a poor prognosis. The scarcity of lymphoid tissue in the breast is a reason for the rarity of primary breast lymphoma in the breast [5-6]. Lymph nodes are located in the breast, especially along the lymph channels, in the upper outer quadrant, close to the axillary region. It is suggested that lymphoid neoplasms are formed from these lymphoid structures [6]. The majority of primary breast lymphomas are B-cell lymphomas; diffuse large B-cell type is most common (40-70%) [2]. Lymphomas developing from MALT in the breast have also been reported [2]. Radiographic images of lymphoreticular system malignancies are not specific. There are no characteristic findings to distinguish them from each other, well-circumscribed benign tumors, carcinomas, or diffuse inflammation [7-8]. For a definitive diagnosis, a tru-cut biopsy or excisional biopsy should be performed and should be supported by immunohistochemical studies. In cases where adequate immunohistochemical examinations cannot be performed in the center in the presence of conflicting data in the pathology reports, it is very important for the differential diagnosis to be evaluated together with the clinic, and biopsy repeats in case of doubt and re-evaluation of the pathology samples in advanced centers.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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